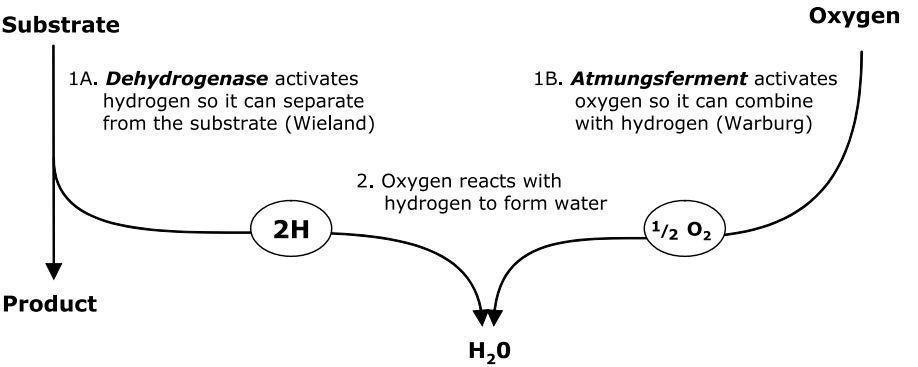

Figure 3.13. Schematic account of how Wieland's account of respiration in terms of dehydrogenation could be linked to Warburg's proposal of an enzyme acting on molecular oxygen.

reaction pathway:

$$\text{Succinic acid} \rightarrow \text{fumaric acid} \rightarrow \text{malic acid} \rightarrow \text{oxaloacetic acid} \rightarrow \text{pyruvic acid} \rightarrow \text{acetic acid.}$$

He then faced a problem in specifying what happened next – it was not possible to remove two hydrogen atoms from acetic acid. In response to this problem, Thunberg offered a bold proposal – he proposed "a reaction in which two acetate molecules are simultaneously each deprived of one hydrogen atom, with the joining of their carbon chains into one. The substance which must therefore form is succinic acid" (1920, passage translated by Holmes, 1986, p. 69). The reaction Thunberg proposed was the following:

$$2CH_3\text{—}COOH \rightarrow COOH\text{—}CH_2\text{—}CH_2\text{—}COOH + H_2.$$

In effect, Thunberg had proposed the cycle of reactions illustrated Figure 3.14.[44]

Fifteen years later Hans Krebs, together with William Johnson, incorporated the core of this idea into the citric acid cycle (also known as the *tricarboxylic acid cycle* and later as the *Krebs cycle*). Instead of two molecules of

[44] A related idea was advanced by Albert Szent-Györgyi (1937) on the basis of his studies adding different four-carbon dicarboxylic acids to suspensions of minced pigeon-breast muscle. He proposed a scheme in which the four-carbon acids are viewed as performing hydrogen transport, not steps in oxidation of carbohydrate:

$$\text{Hydrogendonor} \rightarrow \text{oxaloacetate} \rightarrow \text{malate} \rightarrow \text{fumarate} \rightarrow \text{succinate} \rightarrow \text{cytochrome} \rightarrow \text{oxygen}$$

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